REMARKS

Claim 1 has been amended to clarify the claim language. Dependent claims 3 and 4 were rejected as unclear, specifically whether "the plurality" referred to the test or reference cell Amendment of claim 1 to recite a first number of sequence tags for the test eukaryotic cell and a second number of sequence tags for the reference cell is intended to clarify that "the plurality" of sequence tags is the same for both the test and reference cells although the number of copies of the tags counted for each of the test and reference cells may differ. Thus, for example, the first and second numbers of copies of the tags may be 100 and 200, respectively, and the plurality of tags may be 10. The plurality of tags is a selected parameter. The first and second numbers of copies is what is determined by enumerating, *i.e.,* they are dependent variables. Similar amendments are made to the other independent claims 37, 59, and 75 for the sake of clarity. The scope of these claims is not change by this amendment.

Claim 1 has been further amended to recite that less than 100 % of the sequence tags calculated to be present in the genome of the eukaryotic cell are enumerated. This is supported at paragraph [22] of the specification. ("Thus, far less than 100 % of the sequence tags must be counted to obtain useful information. In fact, less than 50 %, less than 33 %, less than 25 %, less than 20 %, even less than 15 % of the sequence tags calculated to be present in the genome of the eukaryotic cell need be enumerated to obtain useful data.") Independent claims 37, 59, and 75 have been similarly amended with this recitation.

Claims 25-36 have been amended to recite an isolated population of dimers, rather than the individual dimer previously recited. This is supported in Example 7 of the specification, at

18

paragraph 33 and also at paragraph 21.

New claims 86-91 have been added. Claims 86 and 87 are based on original claim 1 and original claims 4 or 7, respectively. Claims 88 and 89 are based on original claim 37 and original claims 41 or 43, respectively. Claims 90 is based on claim 59 and claim 7; and claim 91 is based on claim 75 and claim 7.

Claims 62, 65, and 77-80 have been amended to clarify their intended meaning. The phrase "wherein the size of the window is" has been replaced with the phrase "the window spans about X kb." This is supported *inter alia* by original claims 6-9. A window which spans a fixed length encompasses it.

As a prefatory comment, the office action repeatedly discusses what a cited reference "reads on." This is a misapplication of a term of patent art and may be have led to a misapplication of the prior art.

Prior art "teaches" certain facts. Prior art must teach all elements of the claim, for example, for both anticipation and obviousness. Whether prior art "reads on" or encompasses a claimed element is not relevant. For example, a teaching of the genus halogens may "read on" the species chlorine because it encompasses it. But such a teaching does not anticipate a claim reciting chlorine.

As a second and separate matter, the term "window" as used in the claim does not read on a concatamer of random sequence tags. Windows are an analytical construct which encompass tags with are contiguous in the genome of the eukaryotic cell. Random tag concatamers may be contiguous in a particular clone, but that does not make them contiguous in the genome.

The Rejection of Claims 3-4 Under 35 U.S.C. §112, Second Paragraph

Claims 3-4 are rejected as unclear because it is allegedly unclear if "the plurality of sequence tags" recited refers to the plurality in the test cells or the plurality in the reference cells. This rejection is respectfully traversed.

The "plurality of sequence tags" is first recited as a claim term in independent claim 1, from which claims 3 and 4 depend. The plurality of sequence tags is the same plurality in both the test and reference cells. The plurality of sequence tags is a set of sequence tags wherein the set comprises more than one sequence tag. Moreover, as stated in claim 1, "the plurality of sequence tags are within a window of sequence tags which are calculated to be contiguous in the genome of the species of the eukaryotic cell." Thus, the plurality of sequence tags compared between the test and reference cells is a single set of tags. What may differ between the test and reference cells is the number of <u>copies</u> of the set of tags in a population of tags generated from the cells. Claim 1 has been amended to clarify this meaning.

It is respectfully submitted that claims 3 and 4 are clear in reference to "plurality of sequence tags" because the plurality is the same for both test and reference cells.

Withdrawal of this rejection is respectfully requested.

The Rejection of Claims 1-2, 18, 20, 24-28, 30-36, 59-60, and 84 Under 35 U.S.C. §102(a)

Claims 1-2, 18, 20, 24-28, 30-36, 59-60, and 84 are rejected as allegedly anticipated by Dunn. This rejection is respectfully traversed.

To reject a claim as anticipated, each and every element as set forth in the claim must be either expressly or inherently described in a single prior art reference. *Verdegaal Bros. v. Union*

Oil co. of California, F.2d 628, 631, 2 U.S.P.Q.2d (BNA) 1051, 1053 (Fed. Cir. 1987).

The independent claims of the rejected claim set are claims 1 and 59 Each of these claims has been amended to recite that less than 100% of the sequence tags or pieces of the genome calculated to be present are enumerated. Dunn does not teach this element.

Dunn teaches redundant sampling of his genome signature tags, *i.e.,* he teaches more than 100% sampling. For the tagging enzyme NotI, 122 tags are calculated to be present in the Yersinia genome. See Figure 1, left. For the fragmenting enzyme Bam HI, 1303 tags are calculated to be present. See Figure 1, right. Dunn actually used Bam HI as the fragmenting enzyme to prepare a GST library. Page 1759, column 1, line 1. Dunn reports extraction of 5432 GSTs from the library. Page 1759, column 1, second full paragraph. Thus, Dunn teaches enumeration of 417% of the sequence tags or genomic fragments which are calculated to be present. Dunn does not teach or suggest any method by which a less than 100% enumeration could be accomplished to provide useful results.

Thus, Dunn fails to teach all elements of the independent claims 1 and 59, as amended. All dependent claims which are rejected also share this element. Therefore they, too, are not anticipated by Dunn.

Claims 25-28 and 34-36 are directed to dimers. Claims 30-33 are directed to concatamers of dimers. Contrary to the assertion of the office action, Dunn does not teach the formation of dimers. At page 1757, first full paragraph, Dunn teaches release of *mono*meric GSTs which were then amplified and randomly ligated to form concatamers. Figure 1 shows generation of *mono*meric tags, not dimers. At page 1764, column 2, Dunn teaches conditions to

promote longer concatamers. Dunn teaches that the "resulting clones typically contained 20 to ≥ 40 GSTs." Thus, Dunn does not teach dimers or concatamers of dimers.

Withdrawal of this rejection is respectfully requested.

The Rejection of Claims 1-2, 15, and 59-60 Under 35 U.S.C. §102(a)

Claims 1-2, 15, and 59-60 are rejected as anticipated by Li (WO 02/002805). This rejection is respectfully traversed.

Claims 1 and 59 are the independent claims of this rejected claim set. These claims have been amended to recite that less than 100% of the sequence tags calculated to be present in the genome of the eukaryotic cells are enumerated. Li does not teach this element of the claims. Therefore, Li cannot anticipate these claims as amended.

Li also does not appear to teach the step of comparing found in claims 1 and 59. Claim 1 requires the comparison of a first number which is a sum of numbers of copies of a plurality of individual sequence tags, wherein the plurality of sequence tags are within a window of sequence tags which are contiguous in the genome. Claim 59 similarly requires comparing numbers of pieces of genome within a window of fixed size. It is not apparent that Li teaches these elements of the independent claims. The dependent claims share these elements and are therefore also not anticipated by Li.

Withdrawal of this rejection s respectfully requested because Li fails to teach all elements of the claims.

The Rejection of Claims 5, 15, 29, 37-38, 40-42, 52, 56, 58, 61, 71, 75-76, 81, and 85 Under 35 U.S.C. §103(a)

Assorted claims are rejected as obvious over Velculescu (U.S. Patent No. 6,498,013) in view of Dunn. This rejection is respectfully traversed.

To establish *prima facie* obviousness of a claimed invention, all the claim limitations must be taught or suggested by the prior art. *In re Royka*, 490 F.2d 981, 180 U.S.P.Q. 580 (C.C.P.A. 1974). "All words in a claim must be considered in judging the patentability of that claim against the prior art." *In re Wilson*, 424 F.2d 1382, 1385, 165 U.S.P.Q. 494, 496 (C.C.P.A. 1970). If an independent claim is nonobvious under 35 U.S.C. §103, then any claim depending therefrom is nonobvious. *In re Fine*, 837 F.2d 1071, 5 U.S.P.Q.2d 1596 (Fed. Cir. 1988).

All of the rejected claims (except claim 29) have been amended or their independent claim has been amended to require that less than 100% of the sequence tags or pieces of genomic DNA calculated to be present in the genome of the eukaryotic cell are enumerated. As discussed above, Dunn does not teach this element. Velculescu also does not teach this element. Thus, the cited combination of references fails to establish a *prima facie* case of obviousness for the claims as amended. See *Royka, supra*.

To establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim

limitations. M.P.E.P. §2143.

The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art, not in applicant's disclosure. *In re Vaeck*, 947 F.2d 488, 20 U.S.P.Q.2d 1438 (Fed. Cir. 1991).
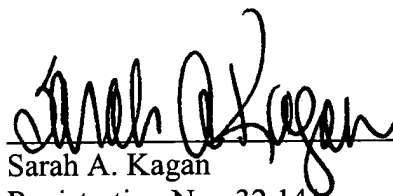
As also discussed above, Dunn does not teach dimers. Velculescu does teach dimers but not of genomic DNA. There is no suggestion or teaching in Dunn that dimers should be used. There is no suggestion or teaching in Velculescu that genomic DNA should be used. Therefore, the cited combination of references fails to establish a *prima facie* case of obviousness for claim 29, because the cited prior art does not teach or suggest the combination. See *Vaeck, supra.*

Withdrawal of this rejection is respectfully requested. Allowance of all pending claims is respectfully solicited.

Respectfully submitted,

Dated: February 16, 2006   By: _____

Sarah A. Kagan
Registration No. 32,141

Banner & Witcoff, Ltd.
Customer No. 22907